Appendix of the Article:

Impact of Primary Health Care on Mortality from Heart and Cerebrovascular Diseases in Brazil: a Nationwide Analysis of Longitudinal Data

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Negative Binomial Regression

A Negative binomial (NB) regression model is used to estimate an outcome that is a given number of events occurring in a fixed interval of time and/or space (e.g., a rate) and the distribution of these rates does not meet those of the Poisson model which requires that the mean is equal to the variance.[1] NB regressions can be used to fit either longitudinal or panel data, where the same unit of analysis has repeated observations over a period of time.[2] In addition to the error term, a term to control for unobserved time-invariant characteristics of the unit of analysis is included. This term can be specified as a fixed or random effect, and the choice between the two, from a statistical point of view, is based on the Hausman specification test.[2,3]

Fixed Effects Models and Impact Evaluations

A fixed effects (FE) specification is an attractive modeling approach because the inclusion of actual terms in the model permits correlations between the unobserved time-invariant term and the explanatory variables.[4] In the current analysis the time-invariant term could represent unobserved characteristics of the municipality (the unit of analysis) which might include geographic, historic, socio-cultural and/or socio-economic characteristics that have a constant value during the period of the study. In FE models the correlation between these characteristics and the treatment variable, in our case the Family Health Program (FHP) coverage, is allowed. Random effects (RE) models are known to be preferable due to greater statistical efficiency however they do not allow the modeling permitted with FE outlined above. For example, if the intervention was implemented with priority in poor areas with a higher disease burden and variables representing or proxy of those characteristics were not measured and consequently not included in the model, the estimates of the effects of the intervention

could suffer from selection bias. FE models allow control for this selection bias using the FE term of the equation to represent these unobserved time-invariant characteristics.[4]

The Regression Model

The regression model used in the present study is as follows:

$Y_{it} = \alpha_i + \beta_1 FHP_{it} + \beta_n X_{nit} + u_{it}$

Where Y_{it} is the age-standardized mortality rate for heart or cerebrovascular diseases for the municipality *i* in year *t*, α_i is the FE for municipality *i* that captures all unobserved time-invariant factors, FHP_{it} was the Family Health Program coverage for the municipality *i* in the year *t*, X_{nit} was the value of each *n* covariate of the model with in the municipality *i* in the year *t,* and u_{it} was the error term.

The time variable

A variable representing time was not included in the model because the mortality rate ratio, comparing two or more groups of coverage exposed to the same mortality time trend, allowed to control for secular trends.[5,6] In order to verify and show that the different FHP coverage were exposed to the same time trend, regression models - stratified according to FHP coverage levels - were fitted using cerebrovascular or heart disease mortality as dependent variables and the time as independent variable. Minimal difference were detected (maximum 2%) and almost all not statistically significant, confirming that time trends along different levels of FHP coverage were similar. This was confirmed by graphical representations (box plots overtime) of these trends. As sensitivity analysis, the same regression models were fitted including a time term both as dichotomous variable (as the other covariates) and dummy variable, as recommended in short equally spaced panel data.[7] The introduction of the time variable eliminated the statistical significance of almost all independent variables (except the FHP when the time was dichotomous), suggesting a problem of over-specification - which tend to increase the SE of the independent variables [8] - or multicollinearity (which was not possible to detect with classical tests for cross-sectional data).

Besides all tests conducted above, the choice of not including the time in the model have been based as well on theoretical considerations. The introduction of a time variable in fixed effects regression models is recommended when there is the suspect that two time series processes are correlated only because they are both trending over time.[3] It has to be considered that in a short panel data such the one used in our study,

characterized by a high number of units of analysis (1622) - which assure a high variability for any variable - and a relatively short period of time (10 years), and with the use of the main socioeconomic CVD determinants, included as ten independent variables in the models, the need of a time variable is reduced in comparison with classical time series studies or long panel data with few units of analysis and few covariates. A time variable is introduced in a model as "artificial variable", representing some unmeasured confounding factor of the association under study, and has no effect itself on CVD mortality rates. It has also to be considered that if the effect of the FHP in the regression models for the CVD was simply due to unmeasured time trends, the same regression models should have shown a positive and statistically significant association of the FHP with the increasing mortality from accidents. On the contrary, no statistically significant effect of FHP was detected.

Considering the statistical tests, the sensitivity analyses and the theoretical reasons described above, a time variable has not been introduced in the final regression models.

Fixed Effects Negative Binomial Regression

Fixed effects negative binomial (FENB) regressions may be estimated using an unconditional or conditional liklihood.[9] Conditional models are implemented in statistical software packages because they can adjust for panels without creating dummy slopes for each panel (as unconditional models do) that is extremely time and computing memory consuming if the number of panels is large. Yet, some studies have suggested that a conditional maximum likelihood estimator of the FENB removes the individual FE only in specific conditions,[9,10] and that the safer alternative, even if time-consuming, is fitting unconditional FENB regressions scaling its standard error (SE) by the Person Chi2 or by the deviance dispersion.[1,9] In order to verify the robustness of our analysis with conditional FENB, we fitted the panel data models using three different model specifications: (1) Conditional FENB, (2) Unconditional FENB with scaled SE, and (3) conditional FE Poisson with robust SE. In TABLE1 we show the models fitted using as the outcome the age-standardized mortality rate for heart and cerebrovascular diseases joined: the estimated effects of FHP (and of the covariates) are almost identical in all these models. The values of two goodness of fit indicators, the Akaike information criterion (AIC) and the Bayesian information criterion (BIC) (that due to their formula was possible to calculate only for the models 1 and 3) suggest that the conditional FENB is the model that better fits the data in comparison to the Poisson regression

model. The same comparison of model specifications have been performed for all the other mortality outcomes of the study: conditional FENB models showed similar effect estimates but better AIC and BIC that Poisson models with robust SE, suggesting that they behave as true FE, on the other hand unconditional FENB models had a problem of convergence in one outcome, the mortality for ischemic heart disease (probably due to the high number of parameters calculated) but in the other outcomes showed very similar values to the conditional FENB.

Difference-in-Difference Analysis

In order to assess the robustness of the fixed-effect multivariate regression models, a difference-in-difference analysis [4] was performed using the municipalities with 0% FHP coverage in 2000 (849), the years 2000 and 2009, and the same FHP coverage levels and covariates used in the FE models.

The results showed a strong and statistically significant effect of FHP, following the gradient of increased FHP coverage for both mortality rates: for the heart diseases coefficients of -5.7, -7.3 and -8.9 and for cerebrovascular diseases -10.5, -10.4 and -11.7 (all statistically significant) for incipient, intermediate and high FHP coverage, respectively.

Propensity Score Analysis

In order to further verify the robustness of our results using matching methodologies, we performed two analyses using the propensity score technique:

1. The evaluation of the average treatment effect on the treated using propensity score matching
2. The introduction of propensity score weights in the same FE multivariate regression models of the study.

Propensity Score Matching (PSM)

The propensity score matching is one of the matching techniques more used in impact evaluations to control for the selection bias in the implantation of an intervention and other bias related to the differences between treated and control.[4,11,12]

Due to the fact that the propensity score has to be estimated at the baseline, before the implementation of the intervention, we used for this analysis the data of the 849 municipalities with 0% FHP coverage in the first year of the study period, the year 2000, as for the difference-in-difference analysis.

The Average Treatment Effect on the Treated (ATT) has been calculated in the last year of the study period, the year 2009, after the full implementation of the intervention in the treated municipalities.

Considering that the PSM does allow only a dichotomous treatment variable, we assigned the control to municipalities with a null (0%) or low (<30%) average FHP coverage during the previous 8 years (the same variable used in previous regression models of table 3 and 4 of the main manuscript), and treated the municipalities with an intermediate or high (>=30%) average FHP coverage in the previous 8 years.

The propensity score of the chance of being treated have been calculated (program psmatch2 in STATA) using all the covariate variables used in the model - as continuous variable - in the baseline year of 2000, when the FHP was not yet implemented in these 849 municipalities. The goodness of matching has been evaluated (program pstest and psgraph in STATA) and the resulting propensity score have been used for the estimation of the (ATT) in the follow-up period, the year 2009, after the implementation of the intervention. The results are presented in Table 2S and 3S. The ATT has been estimated using several matching options (nearest-neighbor matching, radius matching and kernel matching), and the confidence intervals have been calculated by bootstrapping with the asymptotic number of replication (10,000). There MRs in the treated were the same or higher than the control at the baseline, but were significantly lower at the follow-up. All the ATTs estimated by different matching techniques have been in the expected direction (reduction of MRs) and statistically significant in almost all the bootstrapping options (Table 2S).

Propensity Score Weighted FE Regressions

Another way to use the Propensity Score is to weighted the observations according to the PS in a regression model.[4,12] The same methodology has been used in a recent impact evaluation with a very similar study design that ours.[13] Usually the weight for the control is obtained from W=PS/(1-PS), and is W=1 for the treated.[14,15] The same propensity score obtained previously has been introduced in the FENB regression (option iweight in STATA), and the model fitting have been performed for the 849 municipalities in the panel dataset from 2000 to 2009, with the same specifications and covariates of the models used in the study.

The RR on the cerebrovascular mortality of the annual FHP coverage were 0.90 (95%CI:0.88-0.93), 0.86 (95%CI:0.83-0.89) and 0.84 (95%CI:0.80-0.88) for the incipient, intermediate and high FHP coverage, respectively.

The RR on the hearth disease mortality of the annual FHP coverage were 0.94 (95%CI:0.90-0.99), 0.83 (95%CI:0.79-0.87) and 0.82 (95%CI:0.77-0.87) for the incipient, intermediate and high FHP coverage, respectively.

TABLE 1S: Fixed effects Regression Models for the Association Between Age-Standardized Mortality for Cerebrovascular and Heart diseases and FHP Coverage with Different Model Specifications: Brazil, 2000–2009.

Variables	CVD MR, RR (95%CI)		
	1. Conditional FENB	2. Unconditional FENB with scaled SE*[a]	3. Conditional FE Poisson with Robust SE
FHP population coverage			
No FHP (0%)	1	1	1
Incipient (>0% and <30%)	0.98 (0.95-1.00)	0.96 (0.94-0.99)	0.98 (0.94-1.02)
Intermediate (>= 30% and <70%)	0.84 (0.82-0.86)	0.86 (0.84-0.89)	0.84 (0.80-0.89)
Consolidate (>= 70%)	0.81 (0.79-0.84)	0.82 (0.80-0.85)	0.81 (0.77-0.84)
Percentage below poverty line > 15.9%	1.10 (1.08-1.13)	1.09 (1.06-1.12)	1.10 (1.06-1.16)
Per capita income (monthly) > 525BR$	0.96 (0.94-0.99)	0.96 (0.93-0.98)	0.97 (0.93-1.01)
Percentage of individuals having basic household appliances >48.4%	0.96 (0.93-0.99)	0.94 (0.92-0.97)	0.96 (0.93-0.99)
Percentage of individuals living in households with inadequate sanitation >13.8%	1.08 (1.04-1.13)	1.08 (1.04-1.12)	1.08 (1.04-1.12)
Percentage of illiterates among individuals over 15 years old >11.0%	1.09 (1.06-1.12)	1.08 (1.05-1.12)	1.08 (1.05-1.12)
Presence of local hospital beds	0.90 (0.83-0.97)	0.93 (0.86-1.01)	0.93 (0.86-0.99)
Number physicians per 1000 inhabitants > 0.55	0.96 (0.94-0.98)	0.97 (0.95-0.99)	0.97 (0.94-0.99)
Urbanization rate> 76.6%	0.94 (0.89-0.99)	0.96 (0.91-1.01)	0.97 (0.91-1.02)
Percentage of highly educated >4.8%	0.92 (0.90-0.94)	0.91 (0.89-0.94)	0.92 (0.89-0.94)
Presence of Tomography and Ultrasonography	0.87 (0.85-0.88)	0.86 (0.84-0.89)	0.87 (0.83-0.91)
No. of observations	16220	16220	16220
No. of counties	1622	1622	1622
AIC	59,548	*[b]	59,646
BIC	59,655		59,747

*[a] *SE scaled by the Pearson chi-square statistic divided by the residual degrees of freedom*

*[b] *Not possible to be estimated according to the AIC and BIC formula; FENB: Fixed Effects Negative Binomial, FE: Fixed Effect*

Table 2S: Means of the Mortality rates in the control and treatment groups in the baseline year (2000) and in the follow-up year (2009) in the 849 selected municipalities.

Year 2000

- Control group

Variable	Obs	Mean	Std. Dev.
Heart	296	22.49996	18.65766
Cerebrovascul	296	39.70089	23.35113

- Treatment group

Variable	Obs	Mean	Std. Dev.
Heart	553	23.71623	24.30696
Cerebrovascul	553	39.68073	30.6256

Year 2009

- Control group

Variable	Obs	Mean	Std. Dev.
Heart	296	14.2521	13.53979
Cerebrovascul	296	27.40806	16.40264

- Treatment group

Variable	Obs	Mean	Std. Dev.
Heart	553	12.24532	13.80707
Cerebrovascul	553	25.08787	21.05958

Table 3S: Average Treatment Effect on the Treated according to the different Matching using the Propensity Score for the year 2009 in the 849 selected municipalities.

Nearest-Neighbor Matching

Cerebrovascular Diseases

```
Bootstrap statistics                              Number of obs    =       849
                                                  Replications     =     10000

------------------------------------------------------------------------------
Variable     |  Reps  Observed      Bias  Std. Err. [95% Conf. Interval]
-------------+----------------------------------------------------------------
       att   | 1.0e+04 -3.687863  -.313964  1.800126  -7.216472  -.1592544  (N)
             |                                       -7.626932  -.5480398   (P)
             |                                       -6.951914  -.0900331  (BC)
------------------------------------------------------------------------------
```

Heart Diseases

```
Bootstrap statistics                              Number of obs    =       849
                                                  Replications     =     10000

------------------------------------------------------------------------------
Variable     |  Reps  Observed      Bias  Std. Err. [95% Conf. Interval]
-------------+----------------------------------------------------------------
       att   | 1.0e+04 -3.324498  .1676185   1.86832  -6.986781   .3377843   (N)
             |                                       -7.316995   .0882668   (P)
             |                                       -8.322362  -.5049284  (BC)
------------------------------------------------------------------------------

Note:  N   = normal
       P   = percentile
       BC  = bias-corrected
```

Kernel Matching

Cerebrovascular Diseases

```
Bootstrap statistics                              Number of obs    =       849
                                                  Replications     =     10000

------------------------------------------------------------------------------
Variable     |  Reps  Observed      Bias  Std. Err. [95% Conf. Interval]
-------------+----------------------------------------------------------------
        att  | 1.0e+04 -3.961436 -.0035408  1.558278  -7.015974  -.9068977   (N)
             |                                       -7.038909  -.8819353   (P)
             |                                       -7.036673  -.8701629  (BC)
------------------------------------------------------------------------------
```

Heart Diseases

```
Bootstrap statistics                              Number of obs    =       849
                                                  Replications     =     10000

------------------------------------------------------------------------------
Variable     |  Reps  Observed      Bias  Std. Err. [95% Conf. Interval]
-------------+----------------------------------------------------------------
        att  | 1.0e+04 -3.392737   .005312   1.34442  -6.028072  -.7574024   (N)
             |                                       -6.065073  -.8535423   (P)
             |                                       -6.095726  -.9007037  (BC)
------------------------------------------------------------------------------

Note:  N   = normal
       P   = percentile
       BC  = bias-corrected
```

Radius Matching

Cerebrovascular Diseases

```
Bootstrap statistics                              Number of obs    =       849
                                                  Replications     =     10000

------------------------------------------------------------------------------
Variable     |  Reps  Observed      Bias  Std. Err. [95% Conf. Interval]
-------------+----------------------------------------------------------------
         att | 1.0e+04 -3.327297 -.0098539  1.574529   -6.41369  -.2409041   (N)
             |                                        -6.424173  -.3120892   (P)
             |                                        -6.369844  -.2446256  (BC)
------------------------------------------------------------------------------
```

Heart Diseases

```
Bootstrap statistics                              Number of obs    =       849
                                                  Replications     =     10000

------------------------------------------------------------------------------
Variable     |  Reps  Observed      Bias  Std. Err. [95% Conf. Interval]
-------------+----------------------------------------------------------------
        attr | 1.0e+04 -3.274437  .0338697  1.296828  -5.816481  -.7323939   (N)
             |                                        -5.889406  -.8123196   (P)
             |                                        -5.979931  -.9036384  (BC)
------------------------------------------------------------------------------
Note:  N   = normal
       P   = percentile
       BC  = bias-corrected
```

Table 4S: Percentages of the dicotomized independent variables according to FHP levels of coverage: Brazil, 2000 and 2009.

	2000				2009			
	No FHP	Incipient	Intermediate	Consolidate	No FHP	Incipient	Intermediate	Consolidate
Per capita income (monthly in BR$) > 525 BR$	30.3	38.8	22.9	13.0	88.8	87.6	76.9	62.5
Percentage below poverty line > 15.9%	68.8	66.3	79.5	82.0	4.9	13.7	21.7	31.7
Percentage of individuals having basic household appliances >48.4%	33.0	33.4	19.0	15.1	90.2	83.0	72.7	60.2
Percentage of individuals living in households with inadequate sanitation >13.8%	60.0	46.6	68.4	70.5	13.3	22.2	29.9	45.1
Percentage of illiterates among individuals over 15 years old >11.0%	60.7	54.1	75.5	82.0	9.1	15.7	26.2	45.3
Presence of local hospital beds	78.9	89.4	83.4	68.1	69.2	92.2	90.0	77.9
Number physicians per 1000 inhabitants > 0.55	31.5	44.7	31.6	26.2	63.6	73.9	69.8	61.6
Urbanization rate > 76.6	44.5	57.8	37.9	43.1	69.2	68.6	62.1	46.8
Percentage of highly educated among >25y >4.8%	26.4	36.6	18.6	11.4	83.2	88.2	80.3	69.4
Presence of tomography and ultrasonography	2.4	5.9	2.0	0.5	7.7	32.0	17.4	4.2

Table 5S: Means of the Variables in the selected group of municipalities (n.1622) and in the total number of Brazilian municipalities (n.5507) in all the period 2000-2009 (10 years).

All Brazilian Municipalities

Variable	Obs	Mean	Std. Dev.
MR Heart Dis	55070	15.37502	19.85549
MR Cerebrov	55070	29.38474	27.46289
Poverty	55070	33.08456	21.06724
Income	55070	407.7072	217.6786
Threegoods	55070	36.25685	24.27851
Inadequ Sani	55070	27.07446	19.46278
Illiterac	55070	19.29219	11.38859
Hosp beds	55070	91.13383	647.206
Num physic	55070	.5027183	.5324136
Urban Rate	55070	61.23914	22.6104
High school	55070	3.767855	2.877434
Gini Index	55070	.5781251	.0861334
IDH	55070	.7435558	.0828722

Selected Municipalities

Variable	Obs	Mean	Std. Dev.
MR Heart Dis	16220	18.40676	18.39389
MR Cerebrov	16220	34.8597	24.95955
Poverty	16220	19.48278	13.60355
Income	16220	535.3500	182.5709
Threegoods	16220	50.38179	19.3958
Inadequ Sani	16220	17.24992	14.18649
Illiterac	16220	12.39384	6.895643
Hosp beds	16220	127.9033	1034.786
Num physic	16220	.6570953	.5791456
Urban Rate	16220	72.08874	19.29537
High school	16220	5.196679	2.870647
Gini Index	16220	.55582	.0765572
IDH	16220	.7912827	.0551993

Figure 1S: Selected municipalities (1622) according to the quality of vital information

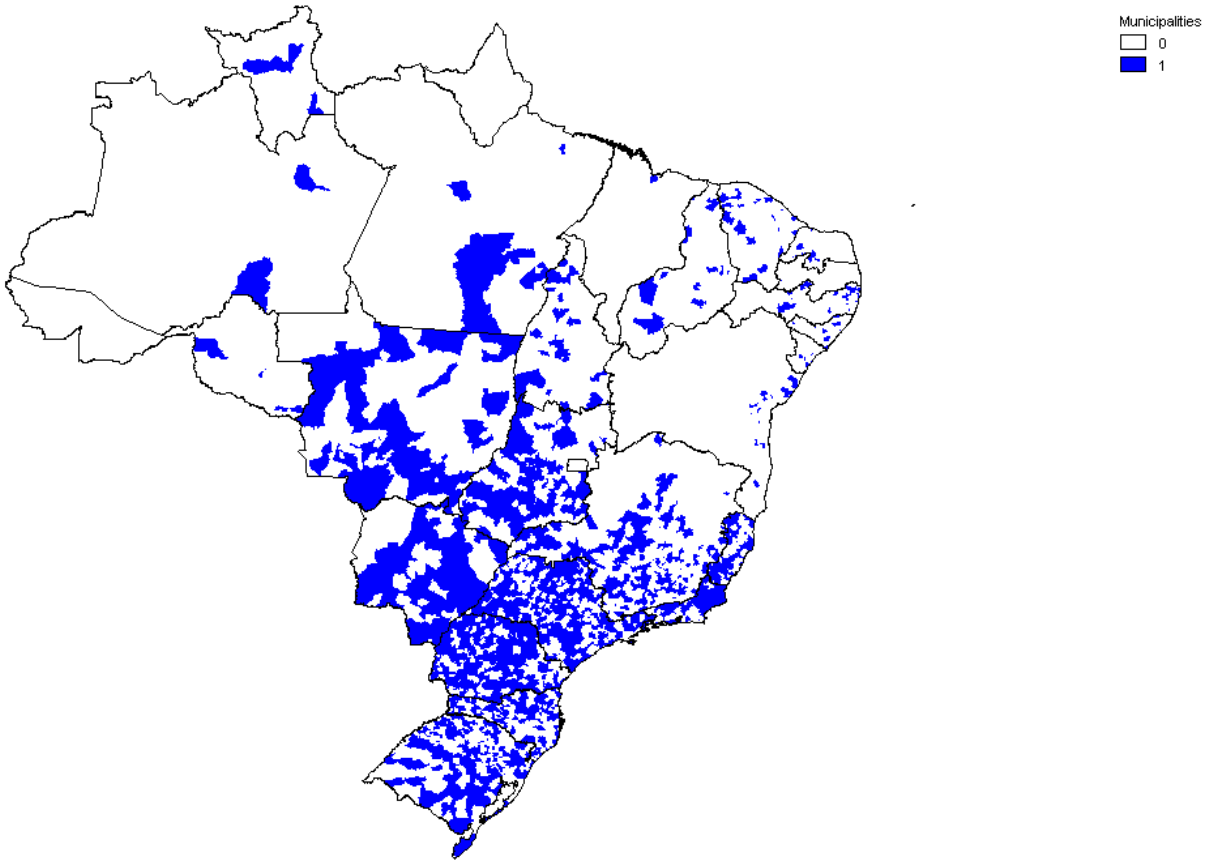
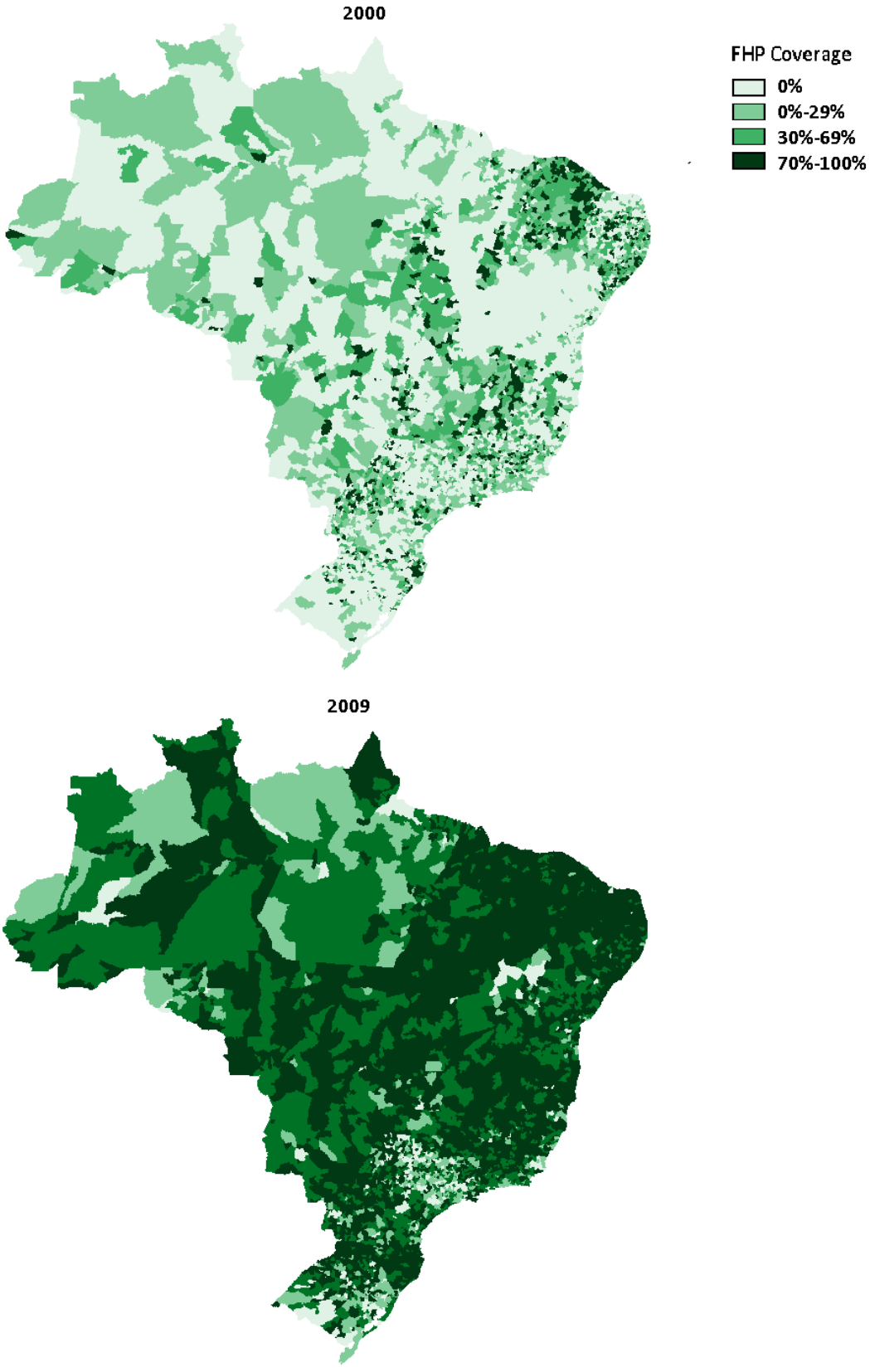


Figure 2S: Coverage levels of the FHP in 2000 and 2009



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